Tumors of the Optic Nerve and Its Sheath

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12.1 Surgical Anatomy of the Optic Nerve

The optic nerve begins within the eyeball at the optic disc and ends in the suprasellar region, where it continues with the chiasm.

Four different parts of the optic nerve may be distinguished: intraocular, intraorbital, intracanalicular, and intracranial [1, 2].

The **intraocular part** is the most anterior component and is located within the eyeball. The optic nerve head, also defined optic disc, is approximatively 1.5 mm wide. The amyelinated fibers are supplied by the central retinal artery.

The **intraorbital part** courses from the posterior part of the eyeball to the intraorbital opening of the optic canal. Its length is about 25 mm. This segment is myelinated and surrounded by three meningeal layers (dura, arachnoid, and pia mater). The subarachnoid space is rather large and narrows posteriorly at the optic canal. Just before it enters the optic canal, the optic nerve is adjacent to the third and the sixth nerves and superomedial to the ophthalmic artery, thus it is closely related to the anulus of Zinn.

The **intracanalicular part** has a variable length from 4 to 10 mm; the optic nerve travels the canal posteromedially at 35° angle relative to the midsagittal plane. This part of the nerve is also covered by the three meningeal layers.

The **intracranial part** extends from the internal orifice of the optic canal to the optic chiasm. It courses in the parasellar region and lies medial to the internal carotid artery, superomedial to the ophthalmic artery, and below the anterior cerebral artery. This segment of the optic nerve is covered only by the pia mater.

12.2 Classification of Tumors of the Optic Nerve and Its Sheath

Many tumors of different histology may involve the optic nerve and its sheath. Some of them primarily arise from the nerve and its sheath; these tumors are

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G. Bonavolontà et al. (eds.), *Cranio-Orbital Mass Lesions*,
https://doi.org/10.1007/978-3-031-35771-8_12

Table 12.1 Classification of primary tumors of the optic nerve and its sheath

Tumors of the optic nerve
• Benign gliomas
• Malignant gliomas
• Ganglioglioma
• Medulloepithelioma
• Hemangioblastoma
Tumors of the optic nerve sheath
• Meningioma
• Schwannoma

discussed in this chapter. In other cases, tumors of the surrounding structures may secondarily involve the nerve. These include meningiomas of the tuberculum sellae, anterior clinoid, planum sphenoidale, gliomas of the optic chiasm and frontal lobe. These cases are excluded from this chapter.

Several cell types may be present in the optic nerve and its sheath. These include astrocytes, oligodendrocytes, fibroblasts, arachnoid cap cells, ganglion cells, Schwann cells of the sympathetic nerves. Thus, several tumors of different histological origin may be observed. They may be classified as in Table 12.1 according to the WHO Classification [3].

12.3 Primary Tumors of the Optic Nerve

12.3.1 Gliomas

Gliomas of the optic nerve occur in two different forms: the more frequent benign gliomas of the pediatric population and the rare malignant gliomas of adults [4–6].

12.3.1.1 Pediatric Benign Gliomas

Optic nerve gliomas account for 2–5% of the central nervous system neoplasms and 7% of all gliomas in pediatric population [7, 8]. They may occur as sporadic lesions or in association to type I neurofibromatosis (NF1). NF1-related tumors occur at younger age (mean 4, 5 years) and are often bilateral [8]. Sporadic tumors are unilateral and occur later, mostly in the first or less in the second decade [7] (Fig. 12.1).

Histologically, pediatric optic nerve gliomas are WHO I pilocytic astrocytomas, rarely diffuse WHO II astrocytomas. Sporadic tumors show higher values of proliferation markers and more aggressive histopathological features.

The biomolecular studies have shown different features between NF1-related and sporadic tumors. The NF1 gene encodes the neurofibromin protein, which functions as tumor suppressor; NF1 dysfunction causes unregulate Ras and m-TOR activity [9]. On the other hand, BRAF mutations are not evidenced in NF1-associated pilocytic astrocytomas but are identified in many sporadic cases [10].

Most optic nerve gliomas are asymptomatic at diagnosis and detected incidentally. However, the clinical course is rather variable; most cases remain stable for years and never grow, while others show visual worsening and slow or more rapid growth pattern over many years [5, 11].

Sporadic optic nerve gliomas are at higher risk of visual loss than those related to the NF1.

Among the non-visual symptoms and signs, proptosis is the most common presenting sign in symptomatic cases. Limitation of the ocular motility and diplopia occur in about 30% of gliomas confined to the orbit whereas they are rare in gliomas of the intracranial optic nerve.

The high incidence of optic nerve glioma in children with NF1 suggests several recommendations for the screening. Children with NF1 and no evident optic nerve glioma should be examined every year up to the age of 18 years. Those with NF1 and history of optic nerve glioma should be studied every 3 months in the first year and every 6 months in the following years.

The vision loss is the most important factor for deciding to treat the glioma, The optic coherence tomography (OCT) is the best study to assess the optic nerve function [12].

Children with sporadic or NF1 optic nerve gliomas and no visual loss must not be treated.

In pediatric patients with substantial tumor progression on MR and/or worsening of visual acuity, chemotherapy is the first-line treatment, particularly in children below 5 years of age [13]. The combination of vincristine and carboplatin has been the most common first-line treatment for optic nerve gliomas. For patients with NF1 who undergo treatment with vincristine/carboplatin, the 3-year progression-free survival (PFS) rate is 77% [14] and the 5-year PFS is 69%, although these cohorts include gliomas beyond

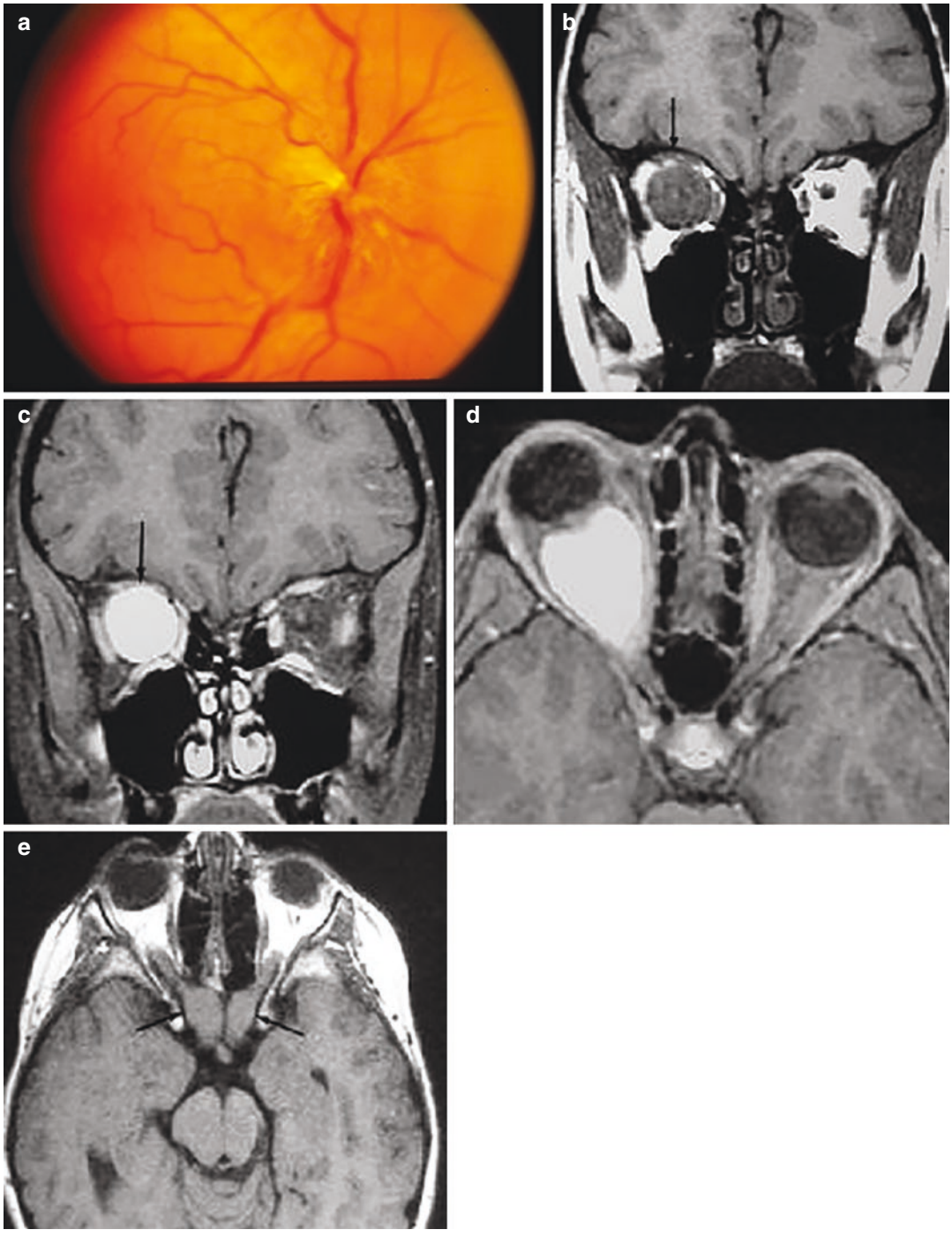

Fig. 12.1 Benign right **optic nerve glioma**. (**a**) Exam of the eye fundus: optic disc with blurred margins. (**b**–**d**) Preoperative magnetic resonance T1 sequences, before (**b**) and after (**c**, **d**) gadolinium: large right intraorbital tumor of the optic nerve with regular margins and homogeneous enhancement; right proptosis is evident. (**e**) Postoperative MR: good tumor resection

the optic nerve. Thioguanine, procarbazine, lomustine, and vincristine may represent a treatment alternative to carboplatin/vincristine in NF1 patients with a reported similar survival [15, 16]. More recently, monotherapies with temozolamide [17], vinblastine [18, 19] and vinorelbine [20] have been used for progressive or refractory disease with positive results and low toxicity.

Surgical debulking is reserved to cases with significant mass effect, aesthetic problems, and no or very limited residual vision. On the other hand, radical surgical resection and radiotherapy represent the last management option in a limited number of patients [11].

The prognosis of optic nerve glioma is rather variable. The features associated to worse outcome include younger age at diagnosis, sporadic tumors, greater contrast enhancement, and extension to the chiasm [8, 21, 22].

12.3.1.2 Malignant Gliomas

Malignant optic nerve gliomas are very aggressive neoplasms occurring in middle-aged males and presenting with rapidly progressive visual loss [4, 15, 23].

The radiological aspect is a mass involving the optic nerve and showing intense contrast enhancement. Histologically, these tumors are anaplastic WHO III astocytomas or glioblastomas (WHO IV). The biopsy is advisable to define the diagnosis.

The tumor progression is very rapid. In the orbit, the tumor infiltrates the meninges of the nerve and the surrounding soft tissues. Gliomas arising from the intracranial optic nerve infiltrate the optic chiasm, hypothalamus, and the surrounding brain.

The management includes combined radiation therapy and chemotherapy [23]. Radiation therapy is a treatment option for patients with malignant optic nerve gliomas and can be used as adjunctive therapy or as an alternative to surgery [24]. Historical series of patients treated with radiation therapy with a total dose of 50–54 Gy given in 1.8–2 Gy per fraction [25–29] reported a local control around 62–89% and overall survival 83–100% at 10 years. The treatment is associated with clinical improvement, including shrinkage of tumor mass and subsequent reduction of proptosis, reduction in optic disc swelling, arrest of progressive visual loss, and improvement of vision. Long-term toxicity reported with the use of conventional radiotherapy includes endocrine abnormalities (13–22%) [1, 27, 28, 30], cerebrovascular disease [31–33], poor visual outcomes (15%) [25–29], secondary malignancies [34, 35], and neurocognitive decline [35], particularly in young patients [26, 36]. Modern techniques have been recently employed to minimize long-term complications of radiation, including fractionated stereotactic radiation therapy [37–39], proton beam radiation therapy [40, 41], and stereotactic radiosurgery (Gamma Knife) [42, 43]. Proton beam therapy has been used for patients with malignant optic nerve gliomas [44]. In a series of 101 patients with malignant optic nerve gliomas receiving photon radiotherapy or proton beam radiotherapy with a total dose of 50.4–54.0 Gy (RBE), Indelicato et al. [44] showed similar progression-free survival and overall survival of 88% and 93%, respectively. The total dose has impact on the local control of the tumors; 54 GyRBE showed a better local control and progression-free survival as compared with a dose less than 54 GyRBE. As for other newly diagnosed high-grade astrocytomas, radiotherapy can be given in combination with temozolomide. Recurrence or progression may be treated with re-resection, a second course of radiotherapy, or most commonly, using systemic alkylating agent chemotherapy [45].

12.3.2 Ganglioglioma

The ganglioglioma, a well-differentiated slow-growing tumor composed of a combination of neoplastic ganglion and glial cells, rarely occurs in the optic nerve [4, 46, 47]. The intracranial optic nerve segment is less rarely affected than the intraorbital one [47]. The association with the NF1 is evidenced in half of the reported cases.

The clinical presentation and the imaging characteristics of ganglioglioma are rather like optic nerve glioma; however, ganglioglioma of the optic nerve causes more rapid, progressive visual failure. Thus, the correct diagnosis is possible only by histological studies.

Most reported gangliogliomas of the optic nerve underwent surgical removal because of the progressive visual loss and potential tumor extension. This management option differs from that of the pilocytic astrocytomas of the optic nerve, where the clinical course is more favorable and the surgical resection is rarely necessary.

Given the rarity of optic nerve gangliogliomas, treatment recommendations are based on evidence or results of the treatment of intracranial gangliogliomas. After a gross total resection is achieved, there is no evidence that adjuvant radiation improves tumor control or patient outcome, and therefore radiation is not recommended in this scenario. After subtotal resection, adjuvant radiation appears to improve local tumor control [48].

12.3.3 Medulloepithelioma

The medulloepithelioma is an embryonal neoplasm, considered in the 2021 WHO classification [3] as subtype of the "embryonal tumors with multilayered rosettes." It rarely occurs in the optic nerve, where it arises from the neuroepithelium that lines the optic vescicles and cavities of the optic nerve [49].

Medulloepithelioma of the optic nerve mainly affects young males and is always malignant. Tumors located in the orbital portion present with proptosis and optic disc swelling, as for optic gliomas; those occurring in more posterior segments of the nerve cause progressive retrobulbar optic neuropathy [4]. The radiological aspect is a fusiform enlargement of the nerve, suggesting an optic glioma.

Most reported cases of optic nerve medulloepithelioma have been treated with tumor excision followed by chemotherapy and radiotherapy. However, the mortality rate is high because of recurrence, CSF spread, and brain invasion [49].

12.3.4 Hemangioblastoma

Hemangioblastomas very rarely occur in the optic nerve, with only 37 reported cases included in two recent reviews [50, 51]. They may occur sporadically or more frequently in association with the Von Hippel Lindau (VHL) disease. The tumor is mostly located in the intraorbital portion of the nerve than in the intracranial one. The reduced vision is the most common presenting symptom, followed by slowly progressive axial proptosis; asymptomatic cases are found incidentally on VHL screening. About one-third of the patients show optic atrophy at initial examination.

The diagnosis is rather easy in VHL patients, but it is difficult in sporadic cases. On MR, the presence of a solid or mixed solid-cystic well-defined lesion within the optic nerve, showing vascular flow voids, intense contrast enhancement and peritumoral edema may suggest the hemangioblastoma.

The best management option of optic nerve hemangioblastomas is controversial. Asymptomatic patients with stable vision should be managed conservatively. However, without treatment most patients will probably lose vision of the affected eye. Surgery is indicated in cases with progressive vision loss, significant proptosis, and bilateral visual symptoms due to edema.

The microsurgical tumor resection is possible, because the optic nerve fibers are dislocated rather than infiltrated. However, it is at risk of visual worsening, particularly for tumors with intracanalicular component. No cases were treated by stereotactic radiosurgery; however, it may be used as alternative option to surgery in advanced cases.

12.4 Tumors of the Optic Nerve Sheath

12.4.1 Meningioma

Optic nerve sheath meningiomas are rare tumors accounting for 1% of all meningiomas and about 2% of all orbital tumors [52, 53]; they are the most frequent tumors of the optic nerve after gliomas. Optic nerve meningiomas are predominant in middle age and in female patients, although they may rarely be found in children in associa-

tion with type II neurofibromatosis (NF2) in one-third of cases. These tumors are usually monolateral (95%) and rarely bilateral (5%) in NF2 patients. The intraorbital portion of the nerve is the most common site of origin (> 90%).

These meningiomas arise from the arachnoid cap cells lining the meningeal optic nerve sheath. They mainly grow circumferentially around the optic nerve and can extent along the entire path of the nerve; other growth patterns include globular, fusiform, and focal enlargement [54]. Histologically, they are benign WHO I, mainly of transitional (50%) or mixed meningothelial-transitional type (30%) [55].

The clinical presentation is characterized by painless and progressive visual loss in the affected eye, which leads to complete blindness, if untreated. Optic disc edema or atrophy are evident. Chronic edema may be associated to posterior tumors causing enlargement of the anterior perioptic subarachnoid space [56]. Visual field defect mainly includes peripheral constriction and enlarged blind spot. Proptosis is inconstant and always follows the visual loss. In pediatric patients, these tumors are more aggressive and result in more rapid visual loss [57].

The diagnosis of optic nerve sheath meningioma is often confirmed by MR with gadolinium-enhanced fat-suppression sequences. The most typical aspect is widening and intense enhancement of the meningeal sheath with central non-enhancing nerve (tram-trak sign) (Fig. 12.2).

The less frequent fusiform enhancement may mimic an optic nerve glioma [54, 58]. Because of the expression of somatostatin receptor subtype 2 by the meningioma cells, the gallium-68 labeled dodecotetracetic acid-tyrosine-3-octreotate positron emission tomography-CT scan may show significant uptake in meningiomas, differently from other tumors [59].

The best management of optic nerve sheath meningiomas depends on the state of visual function and the tumor extension. Cases where the visual function is intact or remains stable should only be observed and closely followed-up by serial ophthalmological examinations and repeated MR every year [58, 60].

The surgical tumor resection results in severe visual loss due to the close tumor relationship to the optic nerve and damage of the pial vascular plexus. Thus, it should be reserved to cases with blind affected eye and disfiguring proptosis or particularly intracranial extension. Patients with blind eye and stable intraorbital tumor may be observed or treated by radiotherapy and operation if the tumor grows. The surgical resection

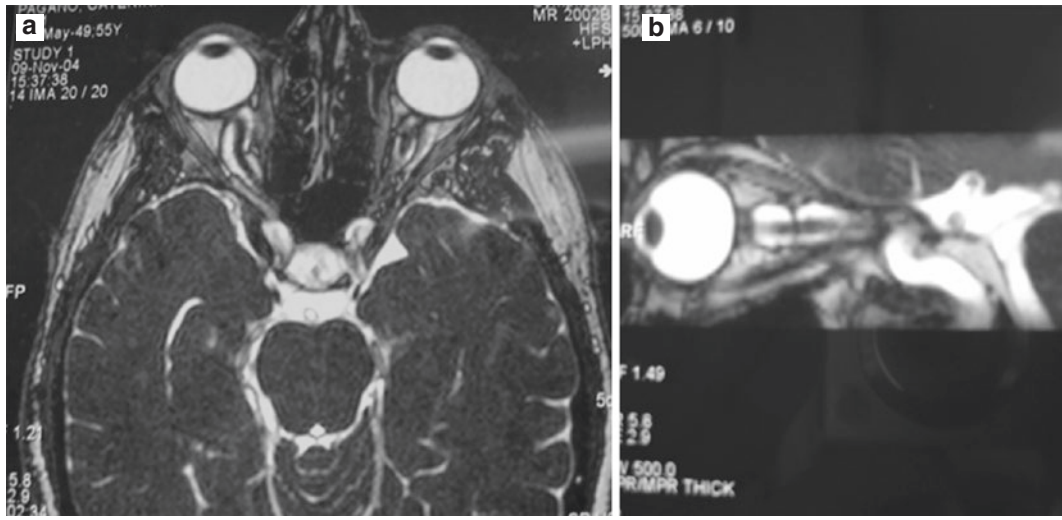

Fig. 12.2 Meningioma of the right intraorbital optic nerve. Magnetic resonance, fat suppression axial (**a**) and post contrast (**b**) sequences: intense contrast enhancement of the meningeal sheath with central non-enhancing nerve (tram-track sign)

may be realized through transcranial approach or lateral orbitotomy [61]. The transnasal endoscopic optic nerve decompression allows to decompress the optic canal and orbital apex, also with the aim to avoid contralateral optic nerve diffusion of the tumor [62, 63]. This less invasive technique shows stabilization of the disease and sometimes improvement of the visual deficit [60, 62, 63].

Radiotherapy is the treatment of choice for most primary optic nerve stealth meningiomas [64]. Current radiation techniques include intensity-modulated radiotherapy [65], stereotactic radiosurgery (SRS) [66], proton beam therapy (PBT) [67], stereotactic fractionated radiotherapy [68]. Such techniques allow better conformal dose to the shape of the tumor significantly reducing the dose to the surrounding healthy organs compared to 3D-conformal RT [69].

A recent meta-analysis comparing different radiotherapy techniques results showed an excellent tumor control rate from 80 to 100% following fractionated radiotherapy using doses of 50–54 Gy in 28–30 fractions of 1.8–2.0 Gy each [70].

Regarding long-term toxicity, three-conformal radiation technique showed a rate of complications higher than more advanced techniques. Reported complication rates using three-conformal radiotherapy, stereotactic fractionated radiotherapy, intensity-modulated radiotherapy, stereotactic radiosurgery, and proton beam radiotherapy were 19% (0–36%), 6% (0–33%), 7% (0–20%), 4.7% (0–4.7%), and 12.5% (0–12.5%), respectively [70]. The most common adverse effect related to RT was retinopathy (44,0.4%), followed by cataract (18%), dry eye (11%), pituitary dysfunction (9%), optic neuritis (6.6%), orbital pain (4.4%), and iritis (4.4%).

12.4.2 Schwannoma

Optic nerve sheath schwannomas are very rare tumors, with only 14 reported cases in recent literature reviews [71–73]. Because the optic nerve is not surrounded by Schwann cells, the origin of these tumors is controversial. The most reliable theory is that they arise from perivascular Schwann cells accompanying the sympathetic nerves innervating the blood vessels of the optic nerve or the central retinal artery. Alternatively, the origin from ectopic Schwann cells may be suggested.

In the reported cases, the clinical presentation is aspecific. At MR, a round homogeneously enhancing tumor in relationship with the optic nerve is evidenced.

Surgery (craniotomy or orbitotomy) has been the primary treatment, allowing large tumor removal; however, the visual prognosis is poor. Fractionated radiotherapy using doses of 45–54 Gy in 28–33 fractions of 1.8 Gy per fraction has been used as complementary treatment in several cases.

12.5 Conclusion

Tumors of the optic nerve and its sheath are mainly gliomas and meningiomas, whereas other oncotypes are exceptional. Most of them are benign and cause slowly progressive visual loss and variable proptosis. The diagnosis of gliomas and meningiomas is usually easy on post-contrast MRI; on the other hand, more rare tumors are diagnosed intraoperatively or at histological examination. Observation is justified in benign tumors with preserved or stable visual function; surgery is often delayed because of the risk of visual worsening, whereas radiation therapy is used in meningiomas and malignant gliomas. However, the visual prognosis is more often poor although with difference according to the tumor type.

References

1. Crumbie L. Optic nerve. https://www.kenhub.com/en/library/anatomy/the-optic-nerve2022.
2. Smith AM. Neuroanatomy, cranial nerve 2 (optic). In: StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing; 2022. https://www.ncbi.nlm.nih.gov/books/NBK507907/.
3. Louis DN, Perry A, Wesseling P, Brat DJ, Cree IA, Figarella-Branger D, et al. The 2021 WHO classifica-

tion of tumors of the central nervous system: a summary. Neuro Oncol. 2021;23(8):1231–51. https://doi.org/10.1093/neuonc/noab106.
4. Miller NR. Primary tumours of the optic nerve and its sheath. Eye (Lond). 2004;18(11):1026–37. https://doi.org/10.1038/sj.eye.6701592.
5. Wladis EJ, Adamo MA, Weintraub L. Optic nerve gliomas. J Neurol Surg B Skull Base. 2021;82(1):91–5. https://doi.org/10.1055/s-0040-1722634.
6. Huang M, Patel J. Optic nerve glioma. In: StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing; 2022. https://www.ncbi.nlm.nih.gov/books/NBK557878/.
7. Beres SJ, Avery RA. Optic pathway gliomas secondary to neurofibromatosis type 1. Semin Pediatr Neurol. 2017;24(2):92–9. https://doi.org/10.1016/j.spen.2017.04.006.
8. Rasool N, Odel JG, Kazim M. Optic pathway glioma of childhood. Curr Opin Ophthalmol. 2017;28(3):289–95. https://doi.org/10.1097/ICU.0000000000000370.
9. Avery RA, Fisher MJ, Liu GT. Optic pathway gliomas. J Neuroophthalmol. 2011;31(3):269–78. https://doi.org/10.1097/WNO.0b013e31822aef82.
10. Yu J, Deshmukh H, Gutmann RJ, Emnett RJ, Rodriguez FJ, Watson MA, et al. Alterations of BRAF and HIPK2 loci predominate in sporadic pilocytic astrocytoma. Neurology. 2009;73(19):1526–31. https://doi.org/10.1212/WNL.0b013e3181c0664a.
11. Farazdaghi MK, Katowitz WR, Avery RA. Current treatment of optic nerve gliomas. Curr Opin Ophthalmol. 2019;30(5):356–63. https://doi.org/10.1097/ICU.0000000000000587.
12. Fard MA, Fakhree S, Eshraghi B. Correlation of optical coherence tomography parameters with clinical and radiological progression in patients with symptomatic optic pathway gliomas. Graefes Arch Clin Exp Ophthalmol. 2013;251(10):2429–36. https://doi.org/10.1007/s00417-013-2394-4.
13. Fisher MJ, Loguidice M, Gutmann DH, et al. Visual outcomes in children with neurofibromatosis type 1-associated optic pathway glioma following chemotherapy: a multicenter retrospective analysis. Neuro Oncol. 2012;14:790–7.
14. Packer RJ, Ater J, Allen J, et al. Carboplatin and vincristine chemotherapy for children with newly diagnosed progressive low-grade gliomas. J Neurosurg. 1997;86:747–54.
15. Ater J, Holmes E, Zhou T, et al. Abstracts from the thirteenth international symposium on pediatric neuro-oncology: results of COG protocol A9952-a randomized phase 3 study of two chemotherapy regimens for incompletely resected low-grade glioma in young children. Neuro-Oncology. 2008;10:451–2.
16. Massimino M, Spreafico F, Cefalo G, et al. High response rate to cisplatin/ etoposide regimen in childhood low-grade glioma. J Clin Oncol. 2002;20:4209–16.
17. Gururangan S, Fisher MJ, Allen JC, et al. Temozolomide in children with progressive low-grade glioma. Neuro Oncol. 2007;9:161–8.
18. Bouffet E, Jakacki R, Goldman S, et al. Phase II study of weekly vinblastine in recurrent or refractory pediatric low-grade glioma. J Clin Oncol. 2012;30:1358–136.
19. Lassaletta A, Scheinemann K, Zelcer SM, et al. Phase II weekly vinblastine for chemotherapy-naive children with progressive low-grade glioma: a Canadian pediatric brain tumor consortium study. J Clin Oncol. 2016;34:3537–43.
20. Cappellano AM, Petrilli AS, da Silva NS, et al. Single agent vinorelbine in pediatric patients with progressive optic pathway glioma. J Neuro-Oncol. 2015;121:405–12.
21. Fisher MJ, Loguidice M, Gutmann DH, Listernick R, Ferner RE, Ullrich NJ, et al. Visual outcomes in children with neurofibromatosis type 1-associated optic pathway glioma following chemotherapy: a multicenter retrospective analysis. Neuro-Oncology. 2012;14(6):790–7. https://doi.org/10.1093/neuonc/nos076.
22. Wan MJ, Ullrich NJ, Manley PE, Kieran MW, Goumnerova LC, Heidary G. Long-term visual outcomes of optic pathway gliomas in pediatric patients without neurofibromatosis type 1. J Neuro-Oncol. 2016;129(1):173–8. https://doi.org/10.1007/s11060-016-2163-4.
23. Alireza M, Amelot A, Chauvet D, Terrier LM, Lot G, Bekaert O. Poor prognosis and challenging treatment of optic nerve malignant gliomas: literature review and case report series. World Neurosurg. 2017;97:751.e1–6. https://doi.org/10.1016/j.wneu.2016.10.083.
24. Marwaha G, Macklis R, Singh AD. Radiation therapy: orbital tumors. Dev Ophthalmol. 2013;52:94–101.
25. Bataini JP, Delanian S, Ponvert D. Chiasmal gliomas: results of irradiation management in 57 patients and review of literature. Int J Radiat Oncol Biol Phys. 1991;21:615–23.
26. Cappelli C, Grill J, Raquin M, et al. Long-term follow up of 69 patients treated for optic pathway tumours before the chemotherapy era. Arch Dis Child. 1998;79:334–8.
27. Grabenbauer GG, Schuchardt U, Buchfelder M, et al. Radiation therapy of optico-hypothalamic gliomas (OHG)–radiographic response, vision and late toxicity. Radiother Oncol. 2000;54:239–45.
28. Horwich A, Bloom HJ. Optic gliomas: radiation therapy and prognosis. Int J Radiat Oncol Biol Phys. 1985;11:1067–79.
29. Jenkin D, Angyalfi S, Becker L, et al. Optic glioma in children: surveillance, resection, or irradiation? Int J Radiat Oncol Biol Phys. 1993;25:215–25.
30. Pierce SM, Barnes PD, Loeffler JS, et al. Definitive radiation therapy in the management of symptomatic patients with optic glioma. Survival and long-term effects. Cancer. 1990;65:45–52.
31. Grill J, Couanet D, Cappelli C, et al. Radiation-induced cerebral vasculopathy in children with neurofibromatosis and optic pathway glioma. Ann Neurol. 1999;45:393–6.

32. Kestle JR, Hoffman HJ, Mock AR. Moyamoya phenomenon after radiation for optic glioma. J Neurosurg. 1993;79:32–5.
33. Tsang DS, Murphy ES, Merchant TE. Radiation therapy for optic pathway and hypothalamic low-grade gliomas in children. Int J Radiat Oncol Biol Phys. 2017;99:642–51.
34. Sharif S, Ferner R, Birch JM, et al. Second primary tumors in neurofibromatosis 1 patients treated for optic glioma: substantial risks after radiotherapy. J Clin Oncol. 2006;24:2570–5.
35. Kim N, Lim DH. Recent updates on radiation therapy for pediatric optic pathway glioma. Brain Tumor Res Treat. 2022;10(2):94–100.
36. Lacaze E, Kieffer V, Streri A, et al. Neuropsychological outcome in children with optic pathway tumours when first-line treatment is chemotherapy. Br J Cancer. 2003;89:2038–44.
37. Combs SE, Schulz-Ertner D, Moschos D, et al. Fractionated stereotactic radiotherapy of optic pathway gliomas: tolerance and long-term outcome. Int J Radiat Oncol Biol Phys. 2005;62:814–9.
38. Marcus KJ, Goumnerova L, Billett AL, et al. Stereotactic radiotherapy for localized low-grade gliomas in children: final results of a prospective trial. Int J Radiat Oncol Biol Phys. 2005;61:374–9.
39. Saran FH, Baumert BG, Khoo VS, et al. Stereotactically guided conformal radiotherapy for progressive low-grade gliomas of childhood. Int J Radiat Oncol Biol Phys. 2002;53:43–51.
40. Fuss M, Hug EB, Schaefer RA, et al. Proton radiation therapy (PRT) for pediatric optic pathway gliomas: comparison with 3D planned conventional photons and a standard photon technique. Int J Radiat Oncol Biol Phys. 1999;45:1117–26.
41. Hug EB, Muenter MW, Archambeau JO, et al. Conformal proton radiation therapy for pediatric low-grade astrocytomas. Strahlenther Onkol. 2002;178:10–7.
42. Liang CL, Lu K, Liliang PC, Chen HJ. Gamma knife surgery for optic glioma. Report of 2 cases. J Neurosurg. 2010;113(Suppl):44–7.
43. El-Shehaby AM, Reda WA, Abdel Karim KM, et al. Single-session gamma knife radiosurgery for optic pathway/hypothalamic gliomas. J Neurosurg. 2016;125:50–7.
44. Indelicato DJ, Rotondo RL, Uezono H, Sandler ES, Aldana PR, Ranalli NJ, et al. Outcomes following proton therapy for pediatric low-grade glioma. Int J Radiat Oncol Biol Phys. 2019;104:149–56.
45. Weller M, van den Bent M, Hopkins K, Tonn JC, Stupp R, Falini A, Cohen-Jonathan-Moyal E, Frappaz D, Henriksson R, Balana C, Chinot O, Ram Z, Reifenberger G, Soffietti R, Wick W. EANO guideline for the diagnosis and treatment of anaplastic gliomas and glioblastoma. Lancet Oncol. 2014;15:e395–403.
46. Wilhelm H. Primary optic nerve tumours. Curr Opin Neurol. 2009;22(1):11–8. https://doi.org/10.1097/WCO.0b013e32831fd9f5.
47. Gacic EM, Skender-Gazibara MK, Gazibara TM, Nagulic MA, Nikolic IM. Intraorbital ganglioglioma of optic nerve in a patient with neurofibromatosis type 1. J Neuroophthalmol. 2012;32(4):350–3. https://doi.org/10.1097/WNO.0b013e318267ff55.
48. Rolston JD, Han SJ, Cotter JA, et al. Gangliogliomas of the optic pathway. J Clin Neurosci. 2014;21:2244–9.
49. Lindegaard J, Heegaard S, Toft PB, Nysom K, Prause JU. Malignant transformation of a medulloepithelioma of the optic nerve. Orbit. 2010;29(3):161–4. https://doi.org/10.3109/01676830903421200.
50. McGrath LA, Mudhar HS, Salvi SM. Hemangioblastoma of the optic nerve. Surv Ophthalmol. 2019;64(2):175–84. https://doi.org/10.1016/j.survophthal.2018.10.002.
51. Darbari S, Meena RK, Sawarkar D, Doddamani RS. Optic nerve hemangioblastoma: review. World Neurosurg. 2019;128:211–5. https://doi.org/10.1016/j.wneu.2019.04.224.
52. Parker RT, Ovens CA, Fraser CL, Samarawickrama C. Optic nerve sheath meningiomas: prevalence, impact, and management strategies. Eye Brain. 2018;10:85–99. https://doi.org/10.2147/EB.S144345.
53. Rassi MS, Prasad S, Can A, Pravdenkova S, Almefty R, Al-Mefty O. Prognostic factors in the surgical treatment of intracanalicular primary optic nerve sheath meningiomas. J Neurosurg. 2018;131(2):481–8. https://doi.org/10.3171/2018.4.JNS173080.
54. Saeed P, Rootman J, Nugent RA, White VA, Mackenzie IR, Koornneef L. Optic nerve sheath meningiomas. Ophthalmology. 2003;110(10):2019–30. https://doi.org/10.1016/S0161-6420(03)00787-5.
55. Jain D, Ebrahimi KB, Miller NR, Eberhart CG. Intraorbital meningiomas: a pathologic review using current World Health Organization criteria. Arch Pathol Lab Med. 2010;134(5):766–70. https://doi.org/10.5858/134.5.766.
56. Arnold AC, Lee AG. Dilation of the perioptic subarachnoid space anterior to optic nerve sheath meningioma. J Neuroophthalmol. 2021;41(1):e100–e2. https://doi.org/10.1097/WNO.0000000000000908.
57. Narayan DS, Traber GL, Figueira E, Pirbhai A, Landau K, Davis G, et al. Natural history of primary paediatric optic nerve sheath meningioma: case series and review. Br J Ophthalmol. 2018;102(8):1147–53. https://doi.org/10.1136/bjophthalmol-2017-310672.
58. Patel BC, De Jesus O, Margolin E. Optic nerve sheath meningioma. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022. https://www.ncbi.nlm.nih.gov/books/NBK430868/Updated. Accessed 24 May 2022.
59. Al Feghali KA, Yeboa DN, Chasen B, Gule MK, Johnson JM, Chung C. The use of 68 Ga-DOTATATE PET-TC in the non invasive diagnosis of optic nerve sheath meningiomas; a case report. Front Oncol. 2018;8:454. https://doi.org/10.3389/fonc.2018.00454.
60. Hénaux PL, Bretonnier M, Le Reste PJ, Morandi X. Modern management of meningiomas compressing the optic nerve: a systematic review.

World Neurosurg. 2018;118:e677–e86. https://doi.org/10.1016/j.wneu.2018.07.020.
61. Kennerdell JS, Maroon JC, Malton M, Warren FA. The management of optic nerve sheath meningiomas. Am J Ophthalmol. 1988;106:450–7.
62. Zoia C, Bongetta D, Pagella F, Antoniazzi ER, Gaetani P. New surgical option for optic nerve sheath meningiomas: fully endoscopic transnasal approach. Can J Ophthalmol. 2018;53(4):e142–e4. https://doi.org/10.1016/j.jcjo.2017.10.020.
63. Maza G, Subramaniam S, Yanez-Siller JC, Otto BA, Prevedello DM, Carrau RL. The role of Endonasal endoscopic optic nerve decompression as the initial management of primary optic nerve sheath meningiomas. J Neurol Surg B Skull Base. 2019;80(6):568–76. https://doi.org/10.1055/s-0039-1677689.
64. Melian E, Jay WM. Primary radiotherapy for optic nerve sheath meningioma. Semin Ophthalmol. 2004;19(3–4):130–40.
65. Bloch O, Sun M, Kaur G, Barani IJ, Parsa AT. Fractionated radiotherapy for optic nerve sheath meningiomas. J Clin Neurosci. 2012;19:1210–5.
66. Marchetti M, Bianchi S, Milanesi I, et al. Multisession radiosurgery for optic nerve sheath meningiomas: an effective option. Preliminary results from a monoinstitutional experience. Neurosurgery. 2011;69:1116–22.
67. Arvold ND, Lessell S, Bussiere M, Beaudette K, Rizzo JF, Loeffler JS, et al. Visual outcome and tumor control after conformal radiotherapy for patients with optic nerve sheath meningioma. Int J Radiat Oncol Biol Phys. 2009;75:1166–72.
68. Soldà F, Wharram B, Gunapala R, Brada M. Fractionated stereotactic conformal radiotherapy for optic nerve sheath meningiomas. Clin Oncol. 2012;24:e106–12.
69. Augspurger ME, Teh BS, Uhl BM, Lee AG, Grant WH, Butler EB, et al. 2091 conformal intensity modulated radiation therapy for the treatment of optic nerve sheath meningioma. Int J Radiat Oncol. 1999;45:324.
70. de Melo LP, Arruda Viani G, de Paula JS. Radiotherapy for the treatment of optic nerve sheath meningioma: a systematic review and meta-analysis. Radiother Oncol. 2021;165:135–41.
71. Ramey WL, Arnold SJ, Chiu A, Lemole M. A rare case of optic nerve schwannoma: case report and review of the literature. Cureus. 2015;7(4):e265. https://doi.org/10.7759/cureus.265.
72. Kashkouli MB, Abdolalizadeh P, Jafari S, Shahrzad S, Karimi N. Is primary optic nerve sheath schwannoma a misnomer? Report of two cases and literature review. Orbit. 2019;38(5):419–23. https://doi.org/10.1080/01676830.2018.1545239.
73. Sharma A, Singh D, Saran R. Primary optic nerve sheath schwannoma: a case report. Br J Neurosurg. 2021:1–3. https://doi.org/10.1080/02688697.2020.1869181.